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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/648,183	08/25/00	BOTSTEIN D	P2533C1

HZ12/0831

GENENTECH INC
ATTN DEIRDE L CONLEY
1 DNA WAY
SOUTH SAN FRANCISCO CA 94080-4990

EXAMINER	
SORBELLO,E	
ART UNIT	PAPER NUMBER
1633	9

DATE MAILED: 08/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/648,183	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Eleanor Sorbello	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to amendment

1. Applicant's amendment and response to the official Office Action mailed December 22, 2000 as Paper No. 4, has been received and filed on June 28, 2001 as Paper No. 8. Claims 27, 29, 30 have been amended. Claims 25-30 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's argument.

2. Applicant's arguments are addressed below on a per section basis.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 25-30 stand rejected under 35 USC § 112, first paragraph for reasons of record, as stated in Office Action dated 12/22/00, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments have been fully considered but they are not persuasive.

Applicants argue (See Response page 4, pagraph 4) that the specification teaches one how to make a knockout animal by homologous recombination of the endogenous gene for ct-1 and an altered genomic DNA for ct-1 introduced into the embryonic cell of the animal. As taught by Mullins,(1996) the resulting mouse would be chimeric and assuming the chimerism extends to the germ line, then an appropriate breeding strategy will lead to the recovery of non-chimeric heterozygotes and if viable, mice which are homozygotes for the genetic change. However, as stated in the Office Action, this method has resulted in the production of knock out mice only, as no other knock out animal has resulted from this method.

Applicants additionally argue that they are enabled for producing any non-human ct-1 knock-out animals (See Response page 4, pagraph 5) and have supplied a reference by Oppenheim et al.(2001) which indicates that viable ct-1 knock-out mice and viable ct-1 heterozygotes were produced as described in the Materials and Methods section of the references. However, the Ct-1 deficient mice as made by Oppenheimer et al. (See Section titled: Generation of Ct-1 deficient mice, paragraph 2) are not distinguishable from the wild-type mice in terms of body weight, respiratory parameters, movement and other behavioral characteristics. Therefore, although this is post filing art, the Ct-1 mice did not indicate any neurological disorder or any cardiac hypertrophy as a phenotype to distinguish it from the wild-type mouse. Therefore the the Ct-1 deficient mouse will not have any use other than being used as a wild-type mouse. Oppenheim also stated that during post-natal life, no obvious abnormalities were detectable upto one year. Oppenheim also stated that the loss of the CT-1 gene

that caused increased motor neuron cell death in embryonic development did not result in any significant change in the post-natal life because Oppenheim et al. teach that the wild-type mouse is indistinguishable from the CT-1 deficient mouse.

However, at the time of filing of the instant application, the prior art did not teach one of skill in the art how to make any transgenic non-human animal knocked out for the ct-1 gene, and neither did the instant application provide guidance to make such an animal, having a phenotype of a specified neurological disorder as the specified pathological condition as in claim 27, or cardiac hypertrophy as in claim 26.

Applicants argue that in view of their arguments the rejection under 35 U.S.C. 112 first paragraph is moot. However, in view of the breadth of the claims, state of the prior art as of the time of filing of the instant application, lack of predictability in the art and lack of guidance in the specification one of skill in the art will require undue experimentation to make and use the instant invention as claimed.

Conclusion

5. Claims 25-30 stand rejected.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eleanor Sorbello whose telephone number is 703-308-6043. The examiner can normally be reached on M-F: 6.30AM-3.00PM.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3230 for regular communications and 703-305-3230 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

August 30, 2001